

MAXWELL (G. T.)

MALARIAL

HÆMOGLOBINURIA

By

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With the Compliments of the Author.

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The phenomena of which I shall treat are commonly called Hæmaturia; but as that term implies hemorrhage and the discharge of blood with urine, it will become evident that it is a misnomer when it is known that the red color of the discharge from the bladder is due not to blood, but to the coloring matter of the blood-hæmoglobine.

It is rare to find red blood-corpuscles in the urinary discharge, and when they are present, they are, except in extreme cases in which the kidneys have become disorganized from congestion, too few to cause the deep color of the urine which is the most striking characteristic of the morbid condition under consideration.

The proof is overwhelming that the destruction of the red blood corpuscles takes place in the general circulation, and that the discharge of red colored urine is not usually the effect of organic lesion of any part of the urinary apparatus.

After citing McHatton, Cochrane, Sternberg and Tyson, the late Dr. R. H. Day, of Baton Rouge, said: "It will be observed by reference to these papers and cases that the one invariable and uniform symptom marking and distinguishing this type of the disease, was the bloody urine, destitute of red blood-corpuscles under the microscope, and presenting a decomposed and disintegrated condition of the red globules. * * * That there is a destruction of the red blood-corpuscles under the action of malarial poison does not seem to be a matter of conjecture, but a pathological fact, demonstrated by rigid microscopical examinations by our best and most experienced pathologists and microscopists."

All the symptoms which characterize the pernicious forms of malarial fever are present in the condition under consideration. But there are, besides, certain conspicuous distinguishing features, viz.: blood-colored urine, a deep yellow color of skin and conjunctivæ, occasional red colored discharges from stomach and bowels, and the filling of vesicles caused by blisters with blood-colored serum. Each and all of these signs and symptoms afford proof that the red blood-corpuscles are disintegrated in the general circulation. They are, indeed, local expressions of a general or constitutional disturbance. We have then Hæmoglobinuria and not Hæmaturia.

There is universal consensus of opinion among intelligent observers and writers that the condition of the blood which gives rise to the signs and symptoms I have described is the effect of malarial poison. Dr. McHatton said: "The etiology of this condition is unquestionably malarial; it only occurs in those who have been for some time exposed to a malarial atmosphere and have given evidences of malarial toxæmia." And Prof. Jones declared that: "Malarial hæmaturia is only one of the forms or varieties of malarial fever, and should not be regarded as a distinct disease dependent for its action

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upon distinct causes. Any case of malarial fever, especially when of long continuance, and without proper nourishment and treatment, may present the phenomena of malarial hæmaturia, in which congestion and hemorrhage of the kidneys supervene." It is for this reason that the adjective *malarial* as a descriptive prefix, has been employed; therefore we have the phrases malarial hæmaturia and malarial hæmoglobinuria applied to the same condition, the latter of which, for reasons given, I have made the title of this paper.

With great surprise I read in Prof. Jones' work, "On Fevers," published in 1887, this statement: "Whilst we have adduced proof to show that this disease, which is only at the present time attracting attention of American physicians, was not unknown to the Grecian, Roman and Arabic physicians; at the same time an extended examination of the medical literature of America since the establishment of medical journals, during the past century, will lead to one of two conclusions, namely:

"First—Malarial hæmaturia was unknown upon the American continent, and had no existence up to 1866.

"Second—Malarial hæmaturia existed, but was not recognized by the medical profession as a distinct form of malarial fever."

You will appreciate the reason for my surprise when you are informed that, in July, 1860, six years before—according to Prof. Jones—the medical profession of America recognized the existence of these striking phenomena as a form of malarial fever, I published a paper upon this subject in the Oglethorpe Medical and Surgical Journal of Savannah, Ga. Therein I described them, and declared that they were not "a new form of disease, but a new symptom, or effect, perhaps, of an old malady."

At the time that my paper was written the literature of the subject was so meagre that it was with great difficulty I could find any evidence that the subject had attracted attention.

In that article I said: "The disease to which the above term (Miasmatic Hæmaturia) has been applied, is one of comparatively recent origin in our midst, and, as well as I can learn was never known anywhere before its appearance in this vicinity (Leon county, Fla., 1850). Not one of several standard works which I have in my library alludes to it, and I am compelled to believe that so striking and alarming a feature of any disease would not have been overlooked by them and the numerous authors whom they quote. Nor has it, until within a few months past, attracted the attention of writers for the medical journals."

Of the contributions which I was successful in finding, one was the translation of a case reported in the Havana Medical Journal, in 1859; and three were reports of cases in the Medical News and Gazette, of New Orleans—one in December, 1859, and two in January, 1860. These reports comprised all the literature that was accessible to me at that time. Since, a great many contributions have appeared in the medical periodicals of the country.

It is peculiarly gratifying to me to find that the views of the etiology and pathology of these interesting phenomena which were ex-

pressed by me, in 1860, have been corroborated by all writers of learning and experience who, in these latter years, have given publicity to their opinions.

Having already made extracts from a few of the highest authorities upon the subject, I will add a quotation from my article, which will show that not only were my views and theirs similar, but that they were identical. I said: "In my judgment, we have in this hemorrhage not a new disease, but a new effect or manifestation of intermittent or remittent fever, of longer or shorter continuance, having recurred more or less frequently; that the subjects have been broken down in health, with a yellowish pallor of complexion and great flaccidness of muscles and tissues generally."

Thus the etiology of the disease has been proven to be malarial; and the pathology to be that which the severest congestive forms of malarial fever present, but in an intensified degree. I have no doubt, however, that the destructive agency of malaria is often assisted by improper treatment, and that profuse purging, especially with the mercurial preparations, has contributed largely to effect the pathological conditions upon which the alarming and dangerous symptoms depend.

The prognosis in this condition is always unfavorable; for such is the extremely prostrated state of the system before these dangerous symptoms supervene, that the power of resistance has been weakened to such a degree that reaction is difficult, even under appropriate treatment. Suppression of urine, which is caused by the disorganized condition of the kidneys from congestion, is almost inevitably fatal. But if the kidneys continue to perform their eliminative function, there is always a probability that under proper treatment recovery will result.

In the matter of treatment there is but a single remedy on which reliance can be placed. I have reference to quinine. It has been demonstrated so often during the last fifty years that the preparations of cinchona are specifics in the various forms of malarial fever that there are now few, if any, who entertain doubt upon the subject.

Before the physiology of the liver and the bile was understood it was the universal belief that that gland and its secretion were in some way the delinquents; and to one or the other, or to both, malarial fevers were attributed. Hence the common appellation, "Bilious Fever." At the same time it was as universally believed that some myterious but specific power to remedy the evil, by removing the cause, attached to the mercurial preparations, particularly to calomel. It was believed that, if the liver was too active and secreted too much bile, or if it was inactive and secreted too little bile, or, whether much or little, if the bile was abnormal in character, calomel, because of a supposed cholagogue action, was the certain curative of the diseased gland, or its abnormal secretion, or, as was supposed, excretion. Then the liver was believed to be the great emunctory—"the *Scavenger*"—of the body, whose especial function was to eliminate effete or poisonous matter, and that poison, it was supposed, was the bile. The liver was regarded as an excretory organ; and the bile was believed to be an excrementitious compound.

Under such views the duty of the physician was, as promptly as possible, to remove the poisonous bile, if excessive, or to stimulate the liver to increased activity if the bile was deficient in quantity, or abnormal in character; and judgment was formed on these matters by an ocular inspection of the fecal discharges. In either case, under every possible condition of the liver and the bile, during fever, the remedy was always the same—calomel.

It was not an unreasonable expectation that, when other and more correct ideas of the physiology of the liver and bile obtained, a change of treatment would result; but I regret to have to say that, though a flood of light has been shed upon the subject, though it has been demonstrated that the liver is not an *excretory* organ, but, on the contrary, that it is the largest and most important *secretory* organ of the body; that bile is not an *excretion*, but is a *secretion*—a digestive compound; that it not only is *not a poison*, but is *essential to the preservation of health and the continuance of life*, without which death from failure of digestion and nutrition is certain and expeditious; that bile is not only not discoverable by the sight, in the fecal discharges, but that it cannot be detected by the most sensitive chemical reagents, *because it is not there*; that, in a word, a complete revolution in the knowledge of the functions and diseases of the liver and the bile has been effected by modern scientists, the practice of “regulating the liver” by the administration of calomel and blue mass still lingers as a ghost of departed error.

On page 792 of the National Dispensatory these sentences will be found: “The belief ^{which} was general and implicit that mercury has some mysterious control over the liver, through which it increased or diminished the secretion of that organ at the physician’s sweet will, has given place to a very general scepticism in regard to the matter; and, indeed, it is asserted that compared with ipecacuanha, aloes, podophylin, euonymin, iodin, sanguinarin, rhubarb, colocynth, senna, scamony and certain sodium salts, mercury manifests the least degree of cholagogue action.” It appears, then, that mercury does not possess the cholagogue power for which it has been, and is, vaunted, and under which mistaken idea it was and is prescribed.

Not only is mercury not curative of malarial fevers, for which, in ignorance of physiology, pathology and therapeutics, it has been so long and so generously administered; but it is positively harmful, in that by its peculiar action it produces the same destructive effects upon the blood that the malarial organism engenders.

On page 724, United States Dispensatory, it is declared that: “While the system is under the action of mercury the blood is more watery than in health, less charged with albumen, fibrine and red-globules, and loaded with a fetid, fatty matter. When drawn from a vein, it exhibits the same appearance as in inflammation.

“In the foregoing observations we have described the ordinary effects of mercury, but occasionally, in peculiar constitutions, its operation is quite different, being productive of a dangerous disturbance of the vital functions.”

I recur to the etiology and pathology of Malarial Hæmoglobinuria

for the purpose of demonstrating the point in the treatment which I wish to emphasize. Whatever may have been, in the past, the conjectures and hypotheses in regard to the cause of malarial fevers, it is now known that a specific germ is the active factor in their causation. And it has been demonstrated with equal certainty that quinine is the germicide of the malarial organism. Blood drawn from a patient during a paroxysm of malarial fever and examined under the microscope, is found to contain malarial germs in the red corpuscles. These germs undergo changes of form in their rapid development and quickly destroy the corpuscles in the general circulation. All the conspicuous phenomena of that class of fevers are, therefore, traced to their action.

The efficient curative effect of quinine in malarial fevers has long been known, but the *modus in quo* this result has been accomplished was until recently a matter of conjecture. Within a few years, however, the germicidal properties of quinine in this class of fevers has been demonstrated; for after its administration, blood in which the red corpuscles had been seen to abound in germs before, has become free from their presence—showing that the organisms had been destroyed by quinine.

In my article (1860), to which allusion has been made, I say: "It will, of course, be anticipated from the views already expressed, that the treatment I have adopted, and would recommend, is that for congestive intermittent fever. Upon quinine, opium, camphor and muriatic tincture of iron I place my chief reliance. * * * Quinine I give in large doses, frequently repeated."

The only addition to the views then expressed I would now make is, that quinine, in case the stomach is is very irritable, should be administered subcutaneously.

I feel pride in stating that, after reading my paper (in 1887), Dr. Dr. McHatton wrote to me: "It shows that you were twenty years ahead of the profession in the matter of treatment."

The argument may be presented syllogistically thus:

- 1st. Quinine is a specific cure for all forms of malarial fever.
- 2d. Malarial Hæmoglobinuria is a form of malarial fever.
- 3d. Therefore, "it follows as the night the day," quinine is the specific cure for malarial hæmoglobinuria.

However, to be quickly and surely remedial, regard must be had to the time of administration of quinine, and to the dose. I have found that to certainly prevent a second paroxysm of any form of malarial fever its use must be begun, regardless of the degree of fever, at the latest by 12 o'clock the day before. Rarely do I pay a second visit, in the milder forms of malarial fever, if I can begin the administration of quinine by that hour. In my early experience I gave unnecessarily large doses. Now I find four grains—at a dose—repeated till twenty-four are taken, ample. In every case, where it is admissible, I combine one of the preparations of opium with quinine.

Beginning at noon, four grains of bi-sulphate of quinine (I prefer that preparation because of its greater solubility and smaller bulk) and one-twelfth grain of morphia, in capsule, are given every

four hours till 12 o'clock at night—to be repeated at 6 and 10 o'clock next morning. If it is feared that a paroxysm may return the second day later than 12 o'clock noon, a capsule is given at 2 o'clock p.m. This treatment will invariably and promptly cure intermittent fever. In remittent fever, and in the congestive form of every type of malarial fever, the remedy must be used early and pressed with greater vigor, the object being to quininize the patient by 12 o'clock at night. For the same reason, when the patient is not seen before noon, the doses must be larger or more frequently repeated till midnight.

I wish to emphasize one other point in the treatment of the common forms of malarial fever, namely: *The absolute necessity that the patient shall be kept quiet in bed the day that the paroxysm is expected to return. Exercise of mind or body will place a favorable result of treatment in jeopardy.* It is because that restriction can be more easily enforced when the patient is under the soporific influence of an opiate that I attach so much importance to the combination of morphia with quinine.

In my early experience I gave no attention to the use of purgatives. It caused me no concern if the bowels were not moved for days. In later years, since I have paid some attention to the study of hygiene—since I have learned that “every person generates enough poison in the alimentary canal every twenty-four hours to destroy life if absorbed”—for the same reason that I urge the daily flushing of municipal sewers, I advocate the daily flushing of the individual sewers—the large intestines—by an efficient purgative. But it matters not what the form of aperient is so that it is efficient. Besides, absorption of the germicide, quinine, is more active after free purgation.

“Tomassi-Crudeli holds that the idea so long held by the medical profession that there is a necessary connection between malarial fevers and marshes, or marshy soils, is thoroughly exploded; the cause of the malarial fevers he declares to be a *specific ferment*, which is not of exclusively palustral origin, and still less of putrefactive processes. In every part of the globe between the two polar circles there are marshes, stagnant waters in which flax and hemp are macerated, and places where the mixture of fresh and salt water takes place on a vast scale, which are not malarious; whilst there are others which are not and never were marshy, and where there is no trace of putrefactive processes, which are malarious in the highest degree. Malaria exists in soils of every conceivable variety, and of every age in geologic time, and it is impossible to point to any micrological or chemical condition of the soil which can be said to be essential.

“From this he argues that all soils have become infected, so to speak, and he defines the word malarious as expressing a soil, or locality, infected by the malarial ferment. We must look to chemical knowledge to guide us in our contests with the specific agents of malaria and other diseases, and we accept the doctrine with but slight modification, that no chemical or other agents can be rightly regarded as disinfectants, in respect of any disease, unless it can be shown to have the power of inhibiting, or arresting the development and

growth of the particular species of microphyte which is the constant concomitant of the morbid process; and that, inasmuch as all specific microphytes are endowed with the power of multiplying in the blood and living tissues of the organism they infest and there playing their part in the morbid processes; all specific disinfectants must, in order to encounter the organisms they are intended to destroy, be of such a nature that they can, without prejudice, be mixed with the circulating blood, and come in contact with the tissues.

"In the case of malarial fevers we have in quinine such a disinfectant, which is not only poisonous to the pathogenic germ of malarial fever, but is, also, of such a nature that it can, without prejudice, be mixed with the blood and come in direct contact with the tissues." (Jones).

In the fall of 1882, I was called hurriedly to a nephew of Col. Adam Eichelberger, at Ocala, who was attacked violently with malarial hæmoglobinuria. Having lost two nephews by the same disease a few years before, who had been treated by the late Dr. Thos. Gary, Col. Eichelberger was greatly alarmed; and as I was temporarily out of my office, Dr. S. Moody was called. Upon reaching the house I found Dr. Moody with the patient, and, after examination, we retired for consultation. Telling Dr. Moody that I proposed to administer quinine and morphia, with greater emphasis than courtesy, he replied: "If you do you will kill him." I answered: "Then I will kill him." "You will excuse me," said Dr. Moody, "if I do not stay to become a party to the homicide." "Certainly," said I, "you are at liberty to withdraw." He left; and I administered quinine and morphine freely. It was the afternoon of Monday. On the next Thursday my patient drove into town; and walked in the next day, Friday. Two years later, in 1884, young Eichelberger had a similar attack at lake Panasoffkee, thirty miles from Ocala. He sent for me, and I pursued the same treatment. Mr. Eichelberger still lives.

The duty of the physician does not end with the arrest of the malarial paroxysms. He must immediately endeavor by reconstructive agents to rectify the effects of the malarial poison primarily upon the blood, and secondarily upon the disabled organs. Iron, especially the muriated tincture, and arsenic should be used persistently after the paroxysms have been arrested.

My conclusions are: First—That the form of Hæmoglobinuria under consideration is essentially a malarial disease, and must be treated upon the general principles which govern in the treatment of all forms of malarial fevers.

Second—That quinine, by its germicidal action, is the certain remedy for all forms of malarial fever.

The failure of quinine in the hands of others is due to improper use of the remedy, as to time and mode of administration, or to the size of doses. It should be borne in mind, however, that if the kidneys are so disorganized by the malarial poison and congestion that suppression of urine and uremic poisoning supervene, death is almost certainly inevitable, under the best treatment.

I take occasion to add, finally, that he who cannot determine the differential diagnosis between malarial and any other form of fever within forty-eight hours, by the effect of quinine, is a stranger to the merits of that invaluable remedial agent, which the late distinguished Dr. Nathan R. Smith, of Baltimore, called "the great civilizer of the nineteenth century."